THE GERM THEORY OF SYPHILIS FROM A CLINICAL POINT OF VIEW.

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THE theory of the microbic origin of syphilis occupies a very peculiar position. No one doubts it and yet although a similar source is proved of many diseases in which but a short time since it was not even suspected and in spite of the fact that many of the ablest investigators have undertaken the task, practically the whole of the evidence upon which it rests is clinical. No pathologist has proved the existence of a germ to the satisfaction of the rest; all the ordinary methods of staining and cultivation have failed to give a convincing result; and no inoculation experiments have succeeded with the exception of a few upon monkeys. Even in the interpretation of the clinical phenomena there are very great difficulties. Recent investigations, however, with regard to the mode of the action of pathogenic germs, and especially the substances formed by them during their growth, have extended our knowledge so far that, although argument from analogy requires to be carefully employed (if there is a germ the conditions under which it thrives are very stringent and possibly it does not belong to the same order as other pathogenic organisms), it may not be unprofitable to consider how far the present standpoint is justified.

1. *The chancre.*—The first difficulty is the existence of a chancre; there is nothing exactly like it in any other microbic disease. It is not the presence of peculiar anatomical features, the intense induration of the base for example, and the sharp definition of the edges; these are easily accounted for by the

specific character of the inflammation, the anatomical structure of the seat of infection, the amount and direction of the connective tissue fibres it contains, and the depth to which the infection is carried at the time of the inoculation; and even if this were not the case there is so far nothing exceptional, for the initial lesions caused by the inoculation of other pathogenic organisms are often distinctive; the peculiar feature is that, with rare exceptions, it can never be produced again. A malignant pustule or a tubercular nodule can develop at any time in any patient suffering from anthrax or tuberculosis no matter what may be the condition of the original point of inoculation; chancre, on the other hand, if the specific induration has once appeared and the disease is still recent, never can (I omit for the present cases of relapsing and recurrent chancre, and those in which reinfection has taken place after some years; they are not as rare as is usually believed, but they are not sufficiently common to invalidate the general argument). A chancre occurs but once; there is no other syphilitic lesion like it; it is never reproduced in the course of the disease; it is never seen among the eruptions of the secondary or tertiary period; and after the induration has once developed, it cannot be produced again even by a fresh inoculation.

This is not due to any alteration the germ has undergone, for inoculation from an entirely fresh source is equally futile; the change is in the tissues, they no longer react in the way they did before the chancre was formed. How this effect is produced is a different matter. Probably it is the result of the action of some chemical substance formed during the growth of the germ, for it affects the whole body, not the locality alone, and its influence is apparent almost from the first day. If inoculation is tried before the induration has developed, during the period that elapses between the original infection and the local manifestation, the incubation period is so shortened that the two chancres attain maturity together.

In other words, tissues that are healthy possess some power of resistance against the syphilitic microbe; there is a long incubation period; growth at first is slow, and even when the germ has gained the lymph stream its extension for some time

is not rapid. Almost, however, from the date of infection the presence of the germ has so great an influence on the tissues that if inoculation is performed a second time either the period of incubation is shortened or the power of local reaction lost altogether.

This cannot be called immunity. There is such a thing as immunity from syphilis, possibly due also to the influence of a chemical product of the germ, but it is different from this. A person cannot be said to be protected from syphilis while suffering from a secondary eruption. Nor can it be called immunity from chancre except in the sense that a person suffering from early syphilis is incapable of developing one.

After a time this peculiar condition subsides; the tissues regain their original power and infection follows its usual course. In some instances only a local sore is formed with more or less of the characteristic induration; in others secondaries make their appearance after the usual time, and occasionally tertiaries as well.

At what period the organism first enters the blood stream is uncertain. As, however, excision or cauterization of the seat of infection almost always fails after the third day, it seems probable that constitutional infection precedes induration. In this case the chancre must be looked upon as a kind of nursery for the germ in the same way that a malignant pustule is for the bacillus of anthrax—the microbe in either case gaining the blood and circulating with it while producing its earliest local changes at the site of the original infection. Unhappily the comparison is incomplete, for while in anthrax destruction of the chief source of the germ materially assists the tissues in dealing with the rest, there is no evidence of any such thing in syphilis.

2. *The secondary period.*—In this there is less difficulty; the organisms continue to accumulate in the blood and the poison to increase in quantity until the well known series of symptoms breaks out. In most cases they are transient; the cellular exudation is small in quantity; the anæmia not serious, and the changes even in the bones chiefly vascular, subsiding readily under treatment. In a few the effects are more grave; the exudation is abundant, as in the tertiary period; the loss

of health very serious, and suppuration and even phagedena may occur. Neither of these is part of the syphilitic process; they may make their appearance at any time, but they are complications due to other kinds of microbes, which find an appropriate soil in the badly nourished and enfeebled tissues of syphilitic patients. Exceptional cases of this nature must be assigned to individual idiosyncrasy—similar occurrences are well known in connection with other specific disorders—for although neglect of treatment or its abuse (there is reason to think that the reckless administration of mercury is especially injurious) may assist, neither is a sufficient explanation by itself.

During the whole of this stage the specific microbe is present in the blood and in the secretion from the cutaneous lesions; they are both intensely infective; but whether the eruptions are the direct product of the germs or of the poisonous subtsances given off by them is uncertain.

3. *The latent period.*—After the secondary symptoms have subsided, the course of the disease is less uniform, and the difficulty of finding an explanation for the clinical phenomena increases. The most striking features are the development of personal immunity and the loss of the power of infection by contact, although (in untreated cases at any rate) that of hereditary transmission persists for many years.

The first of these is, in my opinion, very much overrated. I have known many cases of second infection, a typical one within two years and a half, but immunity, more or less, does exist, and is not to be explained away by saying the patient is syphilitic already, unless that is to say, a similar explanation is allowed for the well known period of immunity after variola, scarlet fever and other specific fevers. Arguing from analogy, it must be the result of some change in the nutrition of the tissues affected by the germ, whether it is the addition of some potent material poured into the blood during the secondary stage, or the exhaustion of something that is essential to the development of the organism. Of the two the former appears the more probable, as it helps to explain the curious protection so often acquired by the mother in cases of heredi-

tary syphilis, and agrees better with what is known of other microbic diseases.

The other peculiarity, the loss of the power of infection by contact, while that of hereditary transmission still persists, can only be explained on the hypothesis that the germ, by continuing to live under the same conditions, has lost some of its original power. The secretion from all secondary eruptions is intensely contagious; that from tertiary ones is not. How long it may be before the power is lost is not known, but there is reason to think that even in cases that are not treated, it dies out by the end of the second year. On the other hand, it is by no means unusual for six or seven miscarriages to occur consecutively, and then for the children who do survive to show signs of the disease, even if ten years have passed. The organism, therefore, is not dead; it has merely lost the power of direct contagion, for if transplanted with the ova or spermatozoa, it springs up into activity again and resumes all its old virulence. The difference between the two phases of its existence is as striking as the alternation of generations in plants and animals.

4. *Hereditary syphilis.*—The phenomena attending inheritance are especially interesting. As the disease is capable of absolutely indefinite multiplication, there can be no doubt that the agent is a living organism. Further it is known that it can be conveyed either through the placenta (as in the case of syphilis acquired late in pregnancy), or through the ova or spermatozoa; but it is equally certain that the disease is very considerably modified. In acquired syphilis the incubation period and the earlier symptoms follow a definite course; in the hereditary form they are much more variable. The lesions may be of the gravest description and prove fatal long before birth, or very mild and give no evidence of their existence for many weeks. In the earlier pregnancies the disease is usually severe; in the latter ones, much milder. In the case of twins one may suffer exceedingly badly, the other but little. In short, although the germ must be the same, its action is widely modified by the conditions under which it is living.

The chief interest is in the law first enunciated by Colles and abundantly verified since. It is one of the best estab-

lished facts in syphilis that a syphilitic child, begotten of a syphilitic father, may be born of a mother who not only shows no sign of the disease herself at the time (tertiaries may make their appearance later), but is apparently incapable of being infected. In other words, the mother is protected without there being any evidence that she is suffering from the disease; and as tertiary affections, although they may occur, are by no means the rule, in a very large proportion of cases the protection is absolute. Arguing from the analogy of other diseases known to be caused by micro-organisms, it has been suggested by Finger and others, that this peculiar immunity is best accounted for by the difference in the relations that exist between the germ and the chemical products it forms during its growth. The specific microbe passes into the ovum and develops in the fœtus; some chemical virus is produced (the same, perhaps, that is the cause of the period of immunity following the secondary stage in acquired syphilis) and this being carried from the fœtus to the mother through the placenta, protects her so thoroughly that infection from her own child after birth is unknown.

If this view is correct, the specific micro-organism in acquired syphilis works its effect before immunity can be established; in the hereditary form, in which the germ is developing under very peculiar conditions, immunity, so far as the mother is concerned, is acquired first.

The chief difficulty is to account for the fœtus frequently suffering severely while the mother escapes. One suggestion is that the organism itself never passes from one to the other (except in those cases in which secondary symptoms break out in the mother); and that consequently only vague general phenomena follow, such as anæmia and loss of health and strength, without any of the characteristic effects. The occasional outbreak of tertiary disorders must then be accounted for on the ground that the germ is not essential to their production. As, however, the organism can pass over as easily as the germs of any other specific disorder, and as it actually does so in a certain proportion of instances, it seems upon the whole more reasonable to suppose that this usually takes place; and that the mother escapes while the fœtus does not,

either because the chemical virus upon which immunity depends passes over more easily than the germ (in the same way that the poison which prevents the development of a chancre spreads over the body long before the germ is able to cause the outbreak of secondaries); or else that, while it can protect the mother thoroughly from secondary eruptions in the fœtus, it is only capable of delaying the outbreak, without preventing it, and prolonging the incubation period.

5. *The outbreak of tertiaries and the relation they bear to other symptoms.*—Tertiary symptoms only occur in a very small proportion of cases, even when treatment is neglected, and they differ from all others in many important particulars. They vary immensely in the date of their origin; they may begin almost at once, or there may be a long interval of perfect health; they have no tendency to get well of themselves; they respond differently to the action of drugs; and although hereditary transmissions may occur during this period, it is not invariable, and probably depends upon the state of health of the individual at the time.

It is generally held that although the later lesions are a consequence of the disease, they are not the direct effect of the germ; that the cause is some peculiar state of nutrition in virtue of which the tissues no longer react to irritants in the ordinary way, but develop gummata instead. This hypothesis, although much may be said in its favor, can scarcely be regarded as satisfactory; it merely states the facts over again in other words; it suggests no reasons for the rarity with which tertiary lesions occur, or for the length of time, passed in many cases in perfect health, that may elapse without a sign of any thing wrong; it presupposes the existence of some irritant other than the syphilitic germ, whenever a tertiary lesion breaks out (unless it is held that the diathesis which has been dormant so many years has at length become sufficient of itself); and it implies that the growth and persistence of gummata can be accounted for merely by a condition of malnutrition.

On the other hand, there are good reasons for believing that in many cases at any rate the germ is present in the tissues and still alive, although, as happens sometimes with tubercle,

it may be latent and require some additional irritant to wake it into life again. Putting aside those instances in which tertiary manifestations occur early in the course of the disease, before the power of contagion is lost, the facts of hereditary transmission are sufficient. The germ, it is true, is greatly modified; it has lost some of its original properties; it acts now as a local irritant, and the tissue changes it causes predominate greatly over the vascular ones; but if by continuing to live under the same conditions, it can lose its power of contagion without altering its nature, there is no great degree of improbability in the supposition that in the same way it may lose the power of affecting the system generally while retaining that of acting local irritant. There are, it is true, one or two points that require explanation if this view is adopted. One is the possibility of reinfection. The period of protection is probably much shorter than is usually believed and a chancre followed by the ordinary symptoms may occasionally be seen side by side with tertiary lesions from some antecedent infection. This, however, does not prove that the original virus is dead; it merely shows that protection is exhausted and susceptibility regained; the specific germ may be there still, unable to cause a general disorder, though it is capable of giving rise to local trouble.

Another has been already mentioned in discussing Finger's hypothesis as to the cause of the immunity acquired by the mother in cases of hereditary transmission. Tertiary symptoms may undoubtedly occur in the mother without there ever having been a chancre or a secondary eruption. This he considers sufficient evidence to prove that they are due to some chemical poison transmitted from the fœtus to the mother in utero, and not to the germ itself. Now, the immunity is a fact, and the occasional occurrence of tertiaries under these conditions must be admitted, but these premises do not by any means entail the conclusion he draws. It is quite as reasonable to suppose that at the time that the chemical virus is carried from the fœtus to the mother to confer immunity on her, the germ which undoubtedly exists in the blood of the fœtus and undoubtedly possesses the power of passing over, may do so too, though it is unable to manifest its influence, owing to the de-

gree of protection already acquired. Then, years later, when the latter has died out, the germ that has remained latent in the tissues may be suddenly roused into activity again and, as in the case of the acquired disease give rise to local symptoms.

6. *The later effects of hereditary syphilis are not easily explained.*—In their general aspects they resemble the ordinary symptoms of the tertiary period and probably if these are dependent upon the local action of the specific micro organism they are dependent upon it too; but there are important differences. Drugs that usually cure tertiary lesions at once have but little influence on many of these, so that if the germ is still living, it must have become still further modified. Many of them are not met with in the acquired form. They nearly always begin, not at irregular intervals, but at one definite time, the commencement of puberty; before this it is exceptional to meet with them; and if this is passed without a sign, they rarely begin afterward. In several cases the development changes that take place at puberty are very much delayed, and often are never thoroughly carried out; the stature remains low; the face retains the appearance of childhood; the pelvis and the figure in the female do not develop; and at twenty the boy or girl retains the appearance of thirteen or fourteen. It seems reasonable to connect these occurrences with each other, and to believe that the sudden outbreak is in some way dependent upon the immense changes that are inaugurated at this time of life; but in the present state of our knowledge it is impossible to do more than associate them together, whether it is thought that the germ is still alive, or that every thing can be accounted for by the profound disorder of nutrition it has left behind it.

7. *Conclusion.*—It must be admitted that a great deal of the preceding is speculative, and that argument from analogy is especially dangerous in the case of syphilis, so little is known with regard to the effect of constitutional peculiarities upon its course. That the original cause is some form of living organism is morally certain; and, if this is admitted, it seems more reasonable to suppose that the later lesions are due to some modification the germ has undergone (it is certainly capable of very extensive ones) rather than to a diathesis which in the

majority of instances only becomes manifest years after the cause has departed. The facts of acquired syphilis agree as well with one theory as the other; those of the hereditary form distinctly favor the former. The most striking deduction from the germ theory is the explanation it offers for Colles' law; and though there is much yet that requires elucidation, especially as regards chancre and late hereditary lesions, there is no doubt that the assumption of the formation of some chemical virus, which may either cause the same symptoms (like tetanin for example), or confer immunity according to the particular conditions under which it is acting, offers the most reasonable explanation for the facts, so far as they are known at present.